PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A sequential multiple assignment randomized trial of a brief contact intervention for suicide risk management among discharged psychiatric patients: an implementation study protocol
AUTHORS	Liu, Hui-ming; Chen, Guanjie; Li, Jinghua; Hao, Chun; Zhang, Bin; Bai, Yuanhan; Song, Liangchen; Chen, Chang; Xie, Haiyan; Liu, Tiebang; Caine, Eric; Hou, Fengsu

VERSION 1 – REVIEW

REVIEWER	Foster, Adriana Telehealth Provider Plus
REVIEW RETURNED	21-Jun-2021

GENERAL COMMENTS	Thank you for the opportunity to review this study protocol. Here are some suggestions on how to present this important study in a clearer, easy to read modality. The title is long and difficult to follow: consider a briefer, clearer version, for example: Development and implementation of Brief Contact study of suicide risk management among discharged psychiatric patients: a sequential multiple assignment randomized trial protocol The clarity of the submission in general can be improved by a professional English language editor who can make such clarity edits. There are also grammar issues that occur quite often in text. The abstract presents two aims as opposed to three aims presented in the body of the manuscript. There are no hypotheses to follow each aim. The first time a hypothesis is mentioned is within the statistical analysis portion of the methods. When presenting the aims each should be followed by a formal hypothesis. It should be briefly stated how each aim will be measured and define the variables. The intervention itself needs to be better fleshed out. The authors state that they had a preliminary study on prevalence of suicidal behavior among patients at the proposed study site. There is no information about their experience or prior attempts to use BCIs. How will the intervention look? We only know it will be implemented on WeChat. The protocol needs a dictionary where the reviewer can quickly get a reference for the abbreviations loke IOF, LHS, etc

	Only Suicidality and Suicidal ideation are proposed as outcomes and instruments are presented for each. How will the completed suicides be determined? For example finding a patient who does not respond to follow up messages? Is there a certain qualitative analysis software program that will be used? How to the authors propose to mitigate the pitfalls? Specifically, if their drop-out is more than 20% or if their recruitment is lagging? Is there a similar hospital they can extend their recruitment to?

REVIEWER	Sreedaran, Priya St John's Medical College Hospital
REVIEW RETURNED	26-Jul-2021

GENERAL COMMENTS	1. This is an important study and I wish the authors all the best in this endeavor. 2. I would request the authors in the introduction to describe more of the existing mental health policies with respect to individuals at risk of suicide in China. That will provide greater justification to the study protocol. For e.g. In page 9 of pdf proof, para 2, line 1, the authors have stated that follow-up is not required for patients with other mental disorders. The authors should note that follow-up policies could vary according to the country. So, I would request the authors to make the necessary changes so readers get a sense of why this study is needed for China and its relevance. 3. The authors should follow a standardized checklist like COREQ if possible for the qualitative part of the study. This will strengthen the study design. Are the authors using a semi-structured questionnaire for their exploring as part of the qualitative study? What kind of analysis are the authors using for the qualitative: thematic/content? The authors have mentioned that they will use purposive sampling but it is not clear from the current manuscript as to where from the authors will recruit the participants? 4. How is the randomization done (in blocks/ or any other format in R? Who does the randomization? The authors need to specify this to ensure that study bias is reduced. 5. Authors cannot mention refusal of consent as an exclusion criterion as one should not consider recruiting participants without informed written consent. Also the authors should specify that participant consent is informed and not just written. 6. For outcomes in qualitative study, the authors should describe cost assessment in greater detail. For e.g. Are they paying study participants for travel and their time as part of this study? In real world, service users might not get paid. Is there a possibility for comparison between treatment as usual arm? 7. The authors need to specify as to what are the criteria for re-randomizing study participants into the more intensive follow-up arm? For e.g how much change in Beck's or MINI Suicidality? 8. Do the authors want to use Incremental Cost effectiveness Ratio (ICER) to compare between the interventions? What type of method do they want to use to calculate ACER?

	9. A crucial limitation is use of predominantly qualitative methods for outcomes like feasibility and acceptability as this could also limit generalizability. 10. While the authors have done a good job in making the manuscript easy to read, however the authors need to perform a grammar check in detail.

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer 1:

1. Thank you for the opportunity to review this study protocol. Here are some suggestions on how to present this important study in a clearer, easy to read modality.

The title is long and difficult to follow: consider a briefer, clearer version, for example:

Development and implementation of Brief Contact study of suicide risk management among discharged psychiatric patients: a sequential multiple assignment randomized trial protocol

Response: Thank you for the advice. We have revised the title of the manuscript as “A sequential multiple assignment randomized trial of a brief contact intervention for suicide risk management among discharged psychiatric patients: an implementation study protocol” on Page 1 Line 1 to 3.

2. The clarity of the submission in general can be improved by a professional English language editor who can make such clarity edits. There are also grammar issues that occur quite often in text.

Response: Thank you for the advice. Now we have worked to improve the quality of the English throughout the manuscript.

3. The abstract presents two aims as opposed to three aims presented in the body of the manuscript.

Response: Thank you for pointing out. We only presented the initial two arms of the sequential multiple assignment randomization in the abstract. Now we have introduced the randomization properly in Abstract on Page 3 Line 15 to Line 18.

4. There are no hypotheses to follow each aim. The first time a hypothesis is mentioned is within the statistical analysis portion of the methods. When presenting the aims each should be followed by a formal hypothesis. It should be briefly stated how each aim will be measured and define the variables.

Response: Thank you for the advice. We briefly presented the context in the prior paragraph of the aims. Now we have revised the paragraph to present the hypothesis more clearly on Page 9 Line 8 to Line 19.

5. The intervention itself needs to be better fleshed out. The authors state that they had a preliminary study on prevalence of suicidal behavior among patients at the proposed study site. There is no information about their experience or prior attempts to use BCIs. How will the intervention look? We only know it will be implemented on WeChat.

Response: Thank you for the comment. We did not have prior attempts to deliver BCIs to discharged patients to reduce their suicide risk. Now we have revised the “Brief contact intervention” section in Method to describe the intervention more clearly from Page 18 Line 19 to Page 19 Line 9, and we have provided an example of the message on WeChat as a Figure 4. Of noted, we have updated in the trial registration and in the manuscript that we will also develop a separate application on smartphones to deliver the message.

6. The protocol needs a dictionary where the reviewer can quickly get a reference for the abbreviations loke IOF, LHS, etc.

Response: Thank you for the comment. Now we have provided a list of abbreviations on Page 31 Line 7 to Page 32 Line 6 .

7. Only Suicidality and Suicidal ideation are proposed as outcomes and instruments are presented for each. How will the completed suicides be determined? For example finding a patient who does not respond to follow up messages?

Response: Thank you for the comment. Completed suicides would be determined during the contacts with participants’ lay health supporters (LHSs). In specific, the research assistants will contact patients at 1, 3, 6 and 12 months after discharge to schedule outpatient visits and complete follow-up surveys. If patients did not respond to the contacts, research assistants will contact their LHSs to obtain participants’ recent updates (including completed suicides) and help them schedule outpatient visits for patients if necessary. At each time point for follow-up survey, if neither patients nor their LHSs responded up to three times, they will be defined as dropout in the study. We have revised the “Quantitative data collection” on Page 19 Line 12 to Page 20 Line 8.

8. Is there a certain qualitative analysis software program that will be used?

Response: In this study, we would not use a certain qualitative analysis software to analysis the data. However, as we will code the qualitative data into the categorical and numerical data, we will

use R program to analyze the numerical data in content analysis. We have revised this on Page 26 Line 6 to 8.

9. How to the authors propose to mitigate the pitfalls? Specifically, if their drop-out is more than 20% or if their recruitment is lagging? Is there a similar hospital they can extend their recruitment to?

Response: Thank you for the comment. The Shenzhen Kangning Hospital (SKH) is a public psychiatric hospital in Shenzhen City. Despite there are general hospitals providing psychiatric outpatient services in Shenzhen, SKH is the only medical facility providing inpatient services to psychiatric patients. There isn't any similar hospital where we can extend the recruitment of discharged participants. We plan to recruit participants in a 6-month period. Considering the SKH has provided inpatient service to 11,590 person-time of inpatients in 2020 and this study plans to recruit participants in a period of 6 months, we believe this study can recruit enough participants. If the recruitment is lagging, we will extend the recruiting period till the sample size is reached. If the drop-out rate was higher than 20% when the trial complete, we will honestly report the dropout rate, the actual power of the trial, investigate its impact and explore possible explanations. We have revised the "Study setting" section on Page 11 Line 20 to Page 12 Line 11 and the "Sample size" section on Page 17 Line 20 to Page 18 Line 7.

Responses to Reviewer 2:

This is an important study and I wish the authors all the best in this endeavor.

1. I would request the authors in the introduction to describe more of the existing mental health policies with respect to individuals at risk of suicide in China. That will provide greater justification to the study protocol. For e.g. In page 9 of pdf proof, para 2, line 1, the authors have stated that follow-up is not required for patients with other mental disorders. The authors should note that follow-up policies could vary according to the country. So, I would request the authors to make the necessary changes so readers get a sense of why this study is needed for China and its relevance.

Response: Thank you for the comment. We sincerely appreciate your advice on illustrating existing mental health policies with respect to individuals at risk of suicide in China, unfortunately, there is no such policy in health system from central, provincial to city/county level. The only policy related to patients' suicide risk was the Code of Practice for the Management and Treatment of Severe Mental Disorders as we mention in the manuscript. And even the policy is focusing on patients with severe mental disorders including schizophrenia, schizoaffective disorder, paranoid psychosis, bipolar disorder, psychotic disorders due to epilepsy, or intellectual developmental disorder with psychotic disorders. According to the Code, psychiatric facilities should report all patients with severe mental disorders in the Information Management System for Severe Mental Disorders at the city level, then to the national system. Then, registered patients will be assessed from level 0 to 5 for the risk of violent

behaviors, in specific, they would be assessed as level 4 if conducted self-harm or attempted suicide; the code requires psychiatrist, family doctors, community mental health workers, community workers and the police to conduct joint follow-ups at least at least once every two weeks for patients at level 3 to 5. However, the follow-ups mainly focus on the risk of violent behaviors towards the public instead of post-discharge suicide. Hence, given the context, we believe it is important to develop and implement an intervention strategy based on brief contact interventions for psychiatric patients at risk of post-discharge suicide risk. We have revised the introduction from Page 6 Line 17 to Page 7 Line 19.

3. The authors should follow a standardized checklist like COREQ if possible for the qualitative part of the study. This will strengthen the study design. Are the authors using a semi-structured questionnaire for their exploring as part of the qualitative study? What kind of analysis are the authors using for the qualitative: thematic/content? The authors have mentioned that they will use purposive sampling but it is not clear from the current manuscript as to where from the authors will recruit the participants?

Response: Thank you for the comment. We have revised the qualitative sections of this study according to the COREQ checklist which will be submitted as supplementary file. The checklist is developed for reporting qualitative research and several items are not applicable at this moment which we have marked as N/A in the file.

We have provided the semi-structured interview questionnaires as a supplementary file in the submission of the revised manuscript. And we will use content analysis for qualitative data.

The patients-LHSs group will be recruited from Shenzhen Kangning Hospital, the clinic mental health service provider group (psychiatrists and nurses, and psycho-crisis intervention team members) will also be recruited from Shenzhen Kangning Hospital, and the community mental health service provider group (community mental health workers and mental health social workers will be recruited from eight community health centers in Shenzhen.

We have revised the manuscript from Page 13 Line 14 to Line 19, Page 14Line 7 to Line 12, and Page 26 Line 6 to Line 8.

4. How is the randomization done (in blocks/ or any other format in R? Who does the randomization? The authors need to specify this to ensure that study bias is reduced.

Response: Thank you for the comment. We now have clearly described in the manuscript that we will use block randomization in R to randomize patients. A statistician in the research team will perform the randomization, and patients, LHSs, nurses who perform recruitment and baseline survey, the statistician who performs randomization, and investigators who perform follow-ups will be blinded

to the randomized assignment. We have revised in the “Randomization and mask” section on Page 18 Line 9 to line 17.

5. Authors cannot mention refusal of consent as an exclusion criterion as one should not consider recruiting participants without informed written consent. Also the authors should specify that participant consent is informed and not just written.

Response: Thank you for the advice. We have revised the manuscript from Page 14 Line 18 to Page 15 Line 5 and Page 16 Line 20 to Page 17 Line 18. We will introduce the study to participants and obtain written informed consent during recruitment, and we have revised related paragraphs on Page 15 Line 7 to Line 12, Page 19 Line 14 to 16, and Page 27 Line 8.

6. For outcomes in qualitative study, the authors should describe cost assessment in greater detail. For e.g. Are they paying study participants for travel and their time as part of this study? In real world, service users might not get paid. Is there a possibility for comparison between treatment as usual arm?

Response: Thank you for the advice. In the qualitative and quantitative study, we will offset participants 100 Yuan (about $15.42) for their efforts and cost of taking part. We have revised the manuscript from Page 15 Line 3 to Line 5 and Page 17 Line 12 to Line 13.

In this study, there will not be a control group as the control/usual arm where participants would receive care as usual, all participants will receive the intervention. Thus, there will not be comparison between treatment group and care-as-usual group.

7. The authors need to specify as to what are the criteria for re-randomizing study participants into the more intensive follow-up arm? For e.g how much change in Beck's or MINI Suicidality?

Response: Thank you for the comment. In this study, the conditions for re-randomization are based on whether the total score of the BSI-CV or the M.I.N.I.-Suicidality will increase, decrease, or remain rather than the exact change. For participants who receive BCIs monthly, if the suicide risk increased, they will be re-randomized to receiving BCIs weekly and bi-weekly, respectively; if the suicide risk decreased or did not change, they will remain receiving BCIs monthly as Group 1c. For participants who receive BCIs weekly, if the suicide risk increased or did not change, they will remain receiving BCIs weekly as Group 2a; if the suicide risk decreased, they will be re-randomized to receiving BCIs monthly and bi-weekly, respectively.

8. Do the authors want to use Incremental Cost effectiveness Ratio (ICER) to compare between the interventions? What type of method do they want to use to calculate ACER?

Response: Thank you for the comment. In this study, all participants will receive the intervention, and there will not be a group of patients as control group receiving care-as-usual, which is very common in randomized trials. Thus, we could not calculate the incremental cost which usually is compared between the intervention group and the control group (care-as-usual). ACER reflects the cost of reducing one unit of post-discharge suicide risk. We plan to use Bootstrap percentile method to calculate ACER. We have revised the manuscript from Page 25 Line 19 to Line 20.

9. A crucial limitation is use of predominantly qualitative methods for outcomes like feasibility and acceptability as this could also limit generalizability.

Response: Thank you for the advice. We have revised the “Discussion” to stress this point on Page 30 Line 17 to Line 20.

10. While the authors have done a good job in making the manuscript easy to read, however the authors need to perform a grammar check in detail.

Response: Thank you for pointing out. We have improved the writing thorough the manuscript.

VERSION 2 – REVIEW

REVIEWER	Foster, Adriana Telehealth Provider Plus
REVIEW RETURNED	20-Sep-2021

GENERAL COMMENTS	The authors efforts to improve the protocol and adopt the reviewer's suggestions are appreciated. The protocol reads better. A few more suggestions are below: 1. Grammar/spelling have improved but issues persist: for example in Figure 1, under Client outcomes box there are several typos 2 Although authors made an attempt to improve, there are no clear hypotheses presented after each study Aim. For example: Hence, our specific aims include: 1) to develop an intervention strategy against post-discharge suicide risk for Chinese psychiatric patients based on BCIs; Here you can introduce a hypothesis based on items presented in section called Implementation evaluation on page 73-74 manuscript with track changes

	2) determine the best delivering frequency of BCIs based on Sequential Multiple 2 Assignment Randomized Trial; for example: do authors think based on existing literature that the weekly BCIs work better? 3) to evaluate the effectiveness of the intervention 3 strategy and explore its implementability under the Implementation Outcome 4 Framework (IOF). Will BCIs decrease suicide risk or increase it?

REVIEWER	Sreedaran, Priya St John's Medical College Hospital
REVIEW RETURNED	01-Oct-2021

GENERAL COMMENTS	The authors have addressed most of the reviewers' concerns. However, on review I would request the authors to address the following queries: 1.The study aims are still not clear in the abstract. 2. Line no 21, page 10: I would request the authors to specify the magnitude of increase on BSIS or MINI that will determine the change to a more intensive BCI. This is necessary as this is a protocol paper and this will contribute to replicability. 3.Line no 6, page 11 "diagnosed with mental disorders, ID...": Kindly mention the classificatory system used for diagnosing with mental disorders. 4. Line no 17, page 18 "we will increase sample size by 20%". Could the authors provide reasons for fixing drop-out rates at 20%? I am aware that the trial is ongoing and the protocol cannot be modified at this juncture but other studies have shown that drop-out rates are higher in this population. 5. Line no 3, page 21: As part of the limitations, the authors should mention that in real world scenarios, it's unlikely that a healthcare system might be able to make so many efforts to reach out to participants. Thus, while this study will provide details of usefulness of BCI in an implementation research framework, in real world, drop-out rates are likely to be much higher. 6. Line no 12, page 22: The authors should specify how they will assess these trajectories. 7. Line no 5, page 26: The authors should clarify adherence to what treatment is being evaluated? Are they evaluating adherence to BCI or prescribed psychiatric treatment? 8. Line no 11, page 27: Can the authors explain in a simpler manner what one unit of post-discharge risk means? 9. Line no 11, page 28: Not sure whether the term 'results' would be the right choice. The term 'inferences' might be more suitable. 10. Could the authors rewrite the discussion with the existing points in a manner that makes it easier to read?

VERSION 2 – AUTHOR RESPONSE

Responses to Reviewer 1:

1. Grammar/spelling have improved but issues persist: for example in Figure 1, under Client outcomes box there are several typos.

Response: Thank you for the advice. We have revised Figure 1 and the manuscript.

2 Although authors made an attempt to improve, there are no clear hypotheses presented after each study Aim.

For example:

Hence, our specific aims include:

1) to develop an intervention strategy against post-discharge suicide risk for Chinese psychiatric patients based on BCIs; Here you can introduce a hypothesis based on items presented in section called Implementation evaluation on page 73-74 manuscript with track changes

2) determine the best delivering frequency of BCIs based on Sequential Multiple 2 Assignment Randomized Trial; for example: do authors think based on existing literature that the weekly BCIs work better?

3) to evaluate the effectiveness of the intervention strategy and explore its implementability under the Implementation Outcome Framework (IOF).

Will BCIs decrease suicide risk or increase it?

Response: Thank you for the advice.

1) The “Implementation evaluation” section in Methods and analysis introduces the outcomes this study will apply to evaluate the implementation of the post-discharge suicide intervention. The first aim of the study is not a hypothesis-driven, instead, it illustrates this study will develop a strategy applying brief contact interventions (BCIs), which are evidence-based effective to reduce post-discharge suicide. The development of the strategy is the very first step to implement the intervention and evaluate outcomes.

2) On Page 9 Line 2 to 12, we have summarized that the different frequencies of implementing BCIs might contribute to the inconsistency in literature. And we hypothesize that “…the frequency was reduced to monthly or bi-monthly, which could consequently be insufficient to maintain the effect on reducing post-discharge suicide risk in a long term.” However, based on current literature, we can only assume that BCIs with more intense delivering frequencies might work better for Chinese

psychiatric patients than BCIs delivered monthly. Thus, we will apply the sequential multiple assignment randomized trial (SMART) to evaluate the effectiveness of BCIs with different sequential delivering frequencies. We have revised the manuscript on Page 9 Line 12 to 14.

3) It is evidence-based that BCIs can reduce suicide risk, and it is not a hypothesis in this study. As mentioned in Page 9 Line 12 to 14, our hypothesis is that BCIs with more intense delivering frequencies might work better for Chinese psychiatric patients than BCIs delivered monthly.

Responses to Reviewer 2:

1.The study aims are still not clear in the abstract.

Response: Thank you for the comment. We have revised the abstract on Page 3 Line 7 to 8.

2. Line no 21, page 10: I would request the authors to specify the magnitude of increase on BSIS or MINI that will determine the change to a more intensive BCI. This is necessary as this is a protocol paper and this will contribute to replicability.

Response: Thank you for the advice. In this study, the re-randomization of participants will be determined by any change, either increase or decrease, in the total score of BSI-CV and MINI. The BSI-C contains 19 items, and each item scores from 0 to 2. The MINI contains 6 items, and “yes” to each item is assigned to score 1, 2, 6, 10, 10 and 4, respectively, otherwise each item will be assigned to 0. Thus, the magnitude of BSI-CV and MINI that will determine the re-randomization is 1 and above. We have specified in the manuscript on Page 16 Line 17 to 18.

3. Line no 6, page 11 "diagnosed with mental disorders, ID...": Kindly mention the classificatory system used for diagnosing with mental disorders.

Response: Thank you for the advice. In this study, participants’ diagnosis will be retrieved from medical records, and the classificatory system used for diagnosing with mental disorders in Shenzhen Kangning Hospital is the International Classification of Diseases 10th Revision (ICD-10). We have revised from Page 11 Line 1 to 2.

4. Line no 17, page 18 "we will increase sample size by 20%". Could the authors provide reasons for fixing drop-out rates at 20%? I am aware that the trial is ongoing and the protocol cannot be modified at this juncture but other studies have shown that drop-out rates are higher in this population.

Response: Thank you for the comment. The prior study, we recruited 689 discharged patients, and 515 of them completed the survey in a three-month follow-up. The drop-out rate was 25.25%. In the prior study, we did not recruit patients' lay health care supporters (LHSs) in the follow-up as an approach to reduce the drop-rate; in comparison, we will recruit patients' LHSs to receive BCIs as well as to help us increase patients' responses and reduce the drop-out rate. Hence, we believe the drop-out rate in the current study will be less than 20%, and we fixed the rate at 20%.

5. Line no 3, page 21: As part of the limitations, the authors should mention that in real world scenarios, it's unlikely that a healthcare system might be able to make so many efforts to reach out to participants. Thus, while this study will provide details of usefulness of BCI in an implementation research framework, in real world, drop-out rates are likely to be much higher.

Response: Thank you for the advice. We agree with you that, in real world, it's unlikely that a healthcare system might be able to make so many efforts to reach out to participants. And this concern is related to sustainability, which we will evaluate in qualitative interviews during the intervention evaluation stage. We have revised the manuscript on Page 14 Line 15 and Page 21 Line 8 to 9. Meanwhile, we are also aware that the mental health providers' attitudes could not fully represent their behaviors. We have revised in the limitation on Page 31 Line 6.

6. Line no 12, page 22: The authors should specify how they will assess these trajectories.

Response: Thank you for the advice. We have revised the manuscript on Page 25 Line 16 to 18 to clarify that we will use Generalized Estimating Equation (GEE) to explore the time-trends/trajectories of repeated measured outcomes and adjust for potential confounding variables.

7. Line no 5, page 26: The authors should clarify adherence to what treatment is being evaluated? Are they evaluating adherence to BCI or prescribed psychiatric treatment?

Response: Thank you for the comment. We will develop a checklist to explore the degree to which the study is implemented as described in the protocol. We have revised the expression and removed the word "adherence" from the manuscript to avoid confusion on Page 21 Line 5 to 7.

8. Line no 11, page 27: Can the authors explain in a simpler manner what one unit of post-discharge risk means?

Response: Thank you for the comment. As we mention on Page10 Line 11 to 13, suicide risk will be evaluated by the Beck Suicide Ideation Scale-Chinese Version (BSI-CV) and the suicidality module of

the Mini-International Neuropsychiatric Interview (M.I.N.I.-Suicidality). And one unit of post-discharge risk refers to one unit of score in BSI-CV and M.I.N.I.-Suicidality. We have revised the manuscript on Page 26 Line 8 to 9.

9. Line no 11, page 28: Not sure whether the term ‘results’ would be the right choice. The term ‘inferences’ might be more suitable.

Response: Thank you for the advice. After discussion, we have revised the term as “qualitative results” on Page 27 Line 8.

10. Could the authors rewrite the discussion with the existing points in a manner that makes it easier to read?

Response: Thank you for the comments. We have revised the discussion based on your advice and comments.